

# High Mortality After Abdominal Operation in Patients With Large-Volume Malignant Ascites

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Advanced intra-abdominal cancers are frequently associated with malignant ascites. The aim of this study was to document the frequency and clinical course of patients found to have large-volume ( $\geq 3$  L) malignant ascites when undergoing a major abdominal operation. Between October 1, 1987 and September 1, 1992, 385 patients with malignant ascites were admitted to hospitals associated with a university medical center. Seventeen with large volume ascites underwent exploration for palliation of bowel obstruction or debulking of tumor. Operative mortality was 41% and mortality correlated with the presence of a nonovarian primary and advanced age. We conclude that patients with large volume nonovarian malignant ascites have a high mortality rate following a major abdominal operation. New approaches such as neoadjuvant or intraperitoneal chemotherapy or possibly peritoneovenous shunt placement at the time of the abdominal operation, are needed to improve the dismal results in this subgroup of patients. © 1996 Wiley-Liss, Inc.

**KEY WORDS:** abdominal tumors, malignant ascites, colon cancer, ovarian cancer

## INTRODUCTION

Advanced intra-abdominal cancers are frequently associated with malignant ascites [1]. Malignant ascites is found in 15–50% of patients with extensive abdominal carcinomatosis [2]. High-volume ascites ( $\geq 3$  L) occurs less frequently. These patients are considered to have advanced disease but often have no other evidence of systemic metastases [3]. Although medical management is often ineffective, large-volume ascites is generally considered a contraindication to major abdominal operation [3]. The large volume ascites contributes to respiratory embarrassment, marked shifts in body fluids, and infection risks that increase surgical mortality.

Malignant ascites is thought to be due to a combination of subdiaphragmatic lymphatic obstruction and increased production of peritoneal fluid [4,5]. Animal studies have shown that subdiaphragmatic lymphatic obstruction alone will not produce ascites [5]. However, at least one patient has been documented to have ascites produced by tumor fluid production alone, without subdiaphragmatic lymphatic obstruction [5]. Because nonsurgical treatment is often ineffective, there may be a role for aggressive surgical cytoreduction with removal of the fluid producing peritoneal deposits.

There is little literature describing the operative course in patients with large volume ascites. Patients with ovarian cancer appear to do well, and treatment is fairly well documented in these patients [6]. Colonic pseudomyxoma can have copious mucinous ascites that responds well to cytoreductive surgery and intraperitoneal chemotherapy [7]. The aim of this study was to document the clinical course of patients found to have high volume malignant ascites when undergoing major abdominal operation. It was hypothesized that patients with malignant ascites from a nonovarian primary would have a higher operative mortality than those with an ovarian primary.

## MATERIALS AND METHODS

Patients at hospitals associated with the University of Missouri who had high-volume ( $\geq 3$  L) ascites and underwent major abdominal operation between October 1, 1987, and September 1, 1992, were identified. The hospitals included the University of Missouri Hospital & Clin-

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**TABLE I. Mortality in Patients After Operation for Large-Volume Malignant Ascites**

Tumor primary	No. of deaths		Total no. of patients
	30 day	90 day	
Ovarian	1	2	8
Nonovarian	6*	7	9
Colorectal	2	2	3
Unknown	1	2	2
Breast	0	0	1
Endometrial	1	1	1
Gastric	1	1	1
Lung	1	1	1

\*  $P < 0.05$  vs ovarian.

ics, Harry S. Truman Memorial Veterans Hospital, and Ellis Fischel Cancer Hospital. Patients were identified using discharge current procedural terminology (CPT) codes, operation records and pathology log books. Seventeen patients with high-volume ascites who underwent surgery were identified and follow-up was completed until death in all patients. Ascites volume of 3 L was chosen based on reports by Holm showing 3–12 L of ascitic fluid in patients described as having massive ascites [2].

These patients were identified among 113,701 total admissions, 73,119 operative procedures, and 92 peritoneovenous shunt placements. Large-volume ascites, defined clinically as a distended abdomen producing discomfort and dyspnea [2] contributed to admission in 427 patients with nonmalignant ascites and 385 patients with malignant ascites during this time period.

The 17 patients underwent exploration for bowel obstruction or tumor debulking. No patients had treatment primarily directed at the ascites with peritoneovenous shunt or ileoentectomy, i.e., small bowel eversion to absorb ascites. The mean age of the patients was 61 years; 10 were female and seven were male.

Patients were analyzed in two groups: those with an ovarian primary ( $n = 8$ ) and those with nonovarian malignancy ( $n = 9$ ). Statistical comparison of continuous data that was normally distributed was done doing the Student's  $t$ -test. Data that may not have been normally distributed were compared using a Wilcoxon rank-sum test. Categorical data was compared with Fisher's exact test. Differences were considered significant at  $P < 0.05$ .

## RESULTS

The tumor primary with perioperative (30-day) and 90-day mortalities are listed in Table I. Patients with nonovarian cancer did poorly with a significantly worse 30-day mortality and a trend toward a worse 90-day ( $P = 0.06$ ) mortality compared to patients with an ovarian primary. Patient parameters by tumor primary and opera-

tive mortality are shown in Table II. Mortality correlated with age, but not with disease-free survival or ascites volume. The cause of operative mortality included sepsis and multisystem organ failure in five patients, myocardial infarction in one, and respiratory failure in one. The two patients who survived the initial operation but died before 90 days succumbed to progression of the underlying cancer. Postoperative chemotherapy was given to 7 patients (ovarian 5, breast 1, colon 1).

Two patients with nonovarian cancer survived longer than 90 days. The patient with breast cancer survived 5 months following abdominal exploration and debulking of tumor. The only patient with colorectal cancer to survive over 30 days was given preoperative neoadjuvant chemotherapy (5-fluorouracil leucovorin). The patient was able to return to work and died 1 year after low anterior resection and debulking of peritoneal metastasis.

## DISCUSSION

This study documents the high operative mortality seen in patients with high-volume malignant ascites due to primary tumors other than ovarian. This high mortality occurred despite careful selection of those patients felt to have a reasonable chance of surviving the perioperative period. Most patients with high volume ascites were not offered surgical therapy during this period. The cause of death was generally sepsis and multiorgan failure, likely hastened by surgical intervention.

The presence of ascites of any volume is a poor prognostic factor in nongynecologic malignancies [3]. In one study all patients with ascites and pancreatic cancer died within 30 days of surgery [3]. The median survival of patients with colorectal cancer and ascites was two months. The poor long-term survival in these patients is similar when they are treated with peritoneovenous shunt. While the shunt has fairly good efficacy in relieving ascites, survival is not improved and is generally measured in weeks [8].

The management of patients with large volume ascites continues to be a major problem. Some recent studies have shown improvement in the patients using systemic [9], or intraperitoneal chemotherapy [10,11], or both [12]. Preliminary work has also been done looking at immunotherapy [13], including monoclonal antibodies [14]. Standard medical management of patients with malignant ascites is generally ineffective. Occasional patients will improve with fluid and sodium restriction, diuretics, and bed rest. Paracentesis can give symptomatic relief but has a transient effect.

The current surgical treatment of nonovarian malignancies with high-volume ascites is clearly unacceptable. New strategies must be developed for these patients. One patient in our study presented with primary colon cancer and massive ascites. Neoadjuvant chemotherapy decreased the ascites and the patient was able to survive

**TABLE II. Parameters According to Tumor Primary and Operative (30-Day) Mortality**

Parameters	Tumor primary		Operative outcome	
	Ovarian	Nonovarian	Died	Survived
Age (yr)				
Range	42-71	44-81	57-81	42-71
Mean $\pm$ SEM	60 $\pm$ 3	63 $\pm$ 4	68 $\pm$ 3	57 $\pm$ 3*
Disease-free interval (mo) <sup>a</sup>				
Range	0-48	0-36	0-12	0-48
Median	7	0	0	2
Survival (days)				
Range	5-1,460	4-365	4-18	32-1,460
Median	199	12**	9	199
Ascites volume (L)				
Range	3-7	3-8	3-8	3-7
Median	5	4	4	5

<sup>a</sup>From time of initial diagnosis of primary tumor.

\*  $P < 0.05$  vs died.

\*\*  $P < 0.05$  vs ovarian.

low anterior resection and peritoneal tumor debulking despite having  $>3$  L of ascites at the time of operation. This experience has encouraged us to consider this option in similar patients.

Another strategy that should be considered is the adjuvant use of peritoneovenous shunts at the time of abdominal operation. The shunt may decrease postoperative ascites and thus ameliorate fluid shifts, early satiety, and respiratory embarrassment seen in the postoperative period. To our knowledge, there are no reports in the literature documenting this as a treatment option. Even though the primary use of peritoneovenous shunts for malignant ascites has limited usefulness [15], using it as an adjuvant at the time of the abdominal operation, may have a beneficial effect.

Surgery plays a critical role in the management of ovarian cancer, even in patients with massive ascites. Postoperative therapy is dependent on the stage and pathology of the tumor. Adjuvant therapy is generally recommended in patients with advanced disease or those patients with stage I disease with unfavorable histology or the presence of ascites. Aggressive cytoreductive surgery is recommended for patients with advanced disease to maximize the subsequent response to chemotherapy. Cisplatin-based combination chemotherapy has been shown to be effective in increasing remission rates and improving median survival. New methods are being evaluated to improve response rates and survival. These include intraperitoneal chemotherapy, and new agents such as Taxol [6].

## CONCLUSIONS

Large-volume malignant ascites in patients with non-ovarian cancer has a high mortality rate with major abdominal surgery. No effective treatments are currently available, although newer chemotherapy and immuno-

therapy may prove useful. New surgical strategies, such as debulking following chemotherapy, or simultaneous debulking and placement of peritoneovenous shunts need to be evaluated.

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